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Title of research project	Development for the evaluation method of immunomodulatory effects of nanomaterials by oral ingestion
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【Abstract】

To assess the adjuvant activity of nano-particle for food use, we attempted to develop the method for evaluation of adjuvant activity of nano- particle using co-culture with human dendritic cells and naïve T cells. Human dendritic cells were stimulated with adjuvants or nano-particles, and cultured with allogenic CD4+CD45RA+ T cells. Then the CD4+ T cells were stimulated with anti-CD3 antibody. The cytokines in the medium were determined using multi-immunoassay system. We developed the in vitro method for evaluation of adjuvant activity of nano- particles using co-culture with human dendritic cells and naïve CD4+ T cells. Nano-particles exhibited no significant activity as a adjuvant on the evaluation of developed method. The results suggested that nano-particles would little affect the dendritic cells as a adjuvant directly.

To investigate the immunomodulatory effect of oral ingested nanomaterials, mice were simultaneously administered with nanomaterials and the antigen protein, ovalbumin for 3 weeks, and we haveobtained ovalbumin-sensitized mice. After challenged by antigen, mice were examined for symptoms including anaphylaxis, antigen-specific antibody titers in the serum, and the population of lymphocytes in Peyer's patches, intestinal lymph nodes and spleen. Increase of antigen-specific antibody titers was observed in mice administered nanosilica particles with a diameter of less than 100 nm. The results suggested that some nanomaterials may have adjuvant activity.

Also, in this study, we measured the particle size and size distribution of a wide range of metal (oxide) nanoparticles in aqueous or biological solutions for clarifying the existence state in foods, the digestion process, absorption and biodistribution. Further, the effect of nanoparticles on induction phase response of skin sensitizing chemicals in vitro was assessed. The skin sensitization response, such as surface antigens expression and chemokines release of immune cells, were not affected by the pre-treatment with nanoparticles. Observations demonstrated that nanoparticles were as agglomerates and/or aggregates in foods. The artificial digestive juices had no effect on their dispersion. Many nanoparticles aggregated in cell culture media and serum. This suggested that it is important to characterize nanoparticles in solution before assessing the in vitro toxicity and to define to accurately assess nanoparticle toxicity.